

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: William Velander *et al.*

Serial No.: 10/049,849

Group No.: 1632

Filed: 06/27/2002

Examiner: Hama, J.

Entitled: **Transgenic Prothrombin And Related Prothrombin Precursors**

**DECLARATION OF DR. WILLIAM VELANDER
UNDER 37 CFR § 1.132**

Mail Stop –Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Examiner Hama:

I, Dr. William Velander, under penalty of perjury, state that:

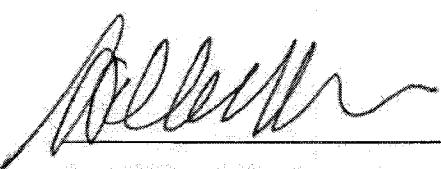
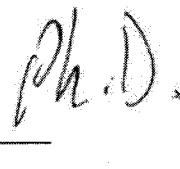
1. I am a co-inventor of the United States patent application captioned above.
2. I am qualified as an expert in the field of protein expression from transgenic mammals.
3. I am a co-author of the references entitled: i) Velander et al., "High-level expression of a heterologous protein in the milk of transgenic swine using the cDNA encoding human protein C" *Proc Natl Acad Sci* 89:12003-12005 (1992); and ii) Van Cott et al., "Transgenic animals as drug factories: a new source of recombinant protein therapeutics" *Expert Opinion On Investigational Drugs* 7:1683-1690 (1998).

6. The data presented in the Velander et al. publication was collected using an immunoassay that detects a particular antigen (i.e., epitope) on the human Protein C pro-enzyme. This antigen is present in both fully carboxylated and partially carboxylated Protein C pro-enzymes. Consequently, the data in Table 1, and discussed on page 12005 1st col. under the "Protein Analysis" section, showing the detection of up to 1000 µg/ml hPC antigen in pig 29-2 is a combination of both fully carboxylated and partially carboxylated hPC. Further, data presented in Velander et al. revealed that less than half (i.e., 38 %) of the detected hPC antigen was fully carboxylated, as measured by anticoagulant activity. *See, pg 12007, col. 1, last two paragraphs.*

5. The discussion within the Van Cott et al. reference provides a citation to the Velander et al. reference that "...the pig was able to γ -carboxylate up to 0.1 g/l/h...". *van Cott et al., pg 1686 rhc – 1687 lhc.* This statement cannot be interpreted that recombinant proteins were fully carboxylated up to concentrations of 0.1 g/l/h. As detailed in Paragraph 4, only 38% of these secreted recombinant proteins were fully carboxylated as determined by anticoagulant activity.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dated: December 22, 2009

Dr. William Velander